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10/581,304	11/02/2006	Hidekazu Tonouchi	Q95291	1881

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EXAMINER	
NIEBAUER, RONALD T	
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1654	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,304	TONOUCHI ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-18* is/are pending in the application.

4a) Of the above claim(s) *17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/30/08; 2/23/07; 6/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I (claims 11-16) and the following peptide: MAP (i.e. SEQ ID NO:1) in the reply filed on 5/29/09 is acknowledged.

Applicants note that claim 15 is missing in the restriction requirement and submit that claim 16 falls within Group I. Applicants are correct. Due to a typographical error, Group I was listed as claims 11-15. However, Group I includes claims 11-16.

Claims 17-18 are to a non-elected group.

Claims 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/29/09.

As discussed below, the elected species was found in the prior art. In accord with section 803.02 of the MPEP the claims have been searched to the extent necessary to determine patentability.

Claims 1-10 have been cancelled.

Claims 11-16 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

37 CFR 1.821(d) states: "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by

"SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application."

In the instant case, page 17 lines 23-25 and page 18 lines 7-10, for example, recite peptides for which a SEQ ID has been provided. However, the sequences are not identified as "SEQ ID NO: " as required by 37 CFR 1.821(d).

Appropriate correction is required.

Information Disclosure Statement

The information disclosure statements filed 2/23/07 and 12/30/08 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because 37 CFR 1.98 b 5 states: "Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication."

In the instant case, the non-patent literature cited for the 12/20/08 does not recite the relevant pages nor the application number. The third non-patent literature cited for the 2/23/07 does not recite the relevant pages nor the application number.

The information disclosure statements filed 2/23/07 and 12/30/08 have been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

The information disclosure statement (IDS) submitted on 6/1/06 has been considered by the examiner. It is noted that the foreign patent documents (which are in a foreign language with no English abstract) and the Sholi Kaneko NPL reference of the IDS 6/1/06 appear in the ISR so as set forth in MPEP section 609.04(a) III a concise explanation of relevance for the non-english references has been provided. All references have been considered.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted that the certified copy of the foreign priority application is not in the English language. Although not an issue at this stage of the examination, it is noted that under certain circumstances, that a translation may be requested (see MPEP 201.15 and 37 CFR 1.55(a)(4)(i)(B)).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a

substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

In the instant case, the claims are drawn to peptides. Claim 11 refers to peptides in which one or more amino acids are added to specific sequences. Claims 11-12 refer to inhibitory activity and claims 15-16 refer to treating certain abnormalities

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of amino acid additions. It is not within the skill of the art to predict any and all additions of amino acids that would result in peptides which inhibit angiotensin-converting enzyme or treat abnormalities of angiotensin-converting enzyme. The art recognizes that structure is not necessarily a reliable indicator of function.

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to peptides. It is noted that adequate written description is provided for claim 11a since claim 11a requires the partial structure Met-Ala-Pro. However, claims 11d-11f and dependent claims are drawn to peptides in which one or more amino acids are added to a sequence. It is noted that no specificity is given as to how many amino acids are added, which amino acids are added, or where the amino acids are added. As such, any peptide of formula (Xaa)n-Met-(Xaa)n-Ala-(Xaa)n-Pro-(Xaa)n, where Xaa is any amino acid and 'n' is any number, falls within the genus of peptides. For example Met-Lys-Lys-Lys-Lys-Lys-Lys-Lys-Lys-Lys-Ala-Lys-Lys-Pro meets the limitation of having amino acids added to SEQ ID NO:1. In considering the size of the genus if one simply considered peptides of formula Met-(Xaa)20-Ala-(Xaa)20-Pro where each Xaa can be any of the 20 naturally occurring amino acids there are at least 20^{40} (i.e.

1099511627776000000000000000000000000000000000000000) different peptides in the genus. As such, the genus is large and does not require a significant structural core.

The specification, for example page 18, refer to 3 peptides that comprise Met-Ala-Pro. However, the peptides represent a small fraction of the possible variety of peptides in the genus. Further, there appear to be no examples in which amino acids have been added between the Met and Ala or between the Ala and Pro residues. One of skill in the art would not recognize that applicant was in possession of the claimed genus.

There is substantial variability in the genus. Since there are a substantial variety of componds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claims 11-12 refer to inhibitory activity and claims 15-16 refer to treating certain abnormalities. However, there is no specific disclosed correlation between structure and function. It is unclear what structural elements are required for the recited function. There are no common attributes or characteristics that identify angiotensin-converting enzyme inhibitors. As such, one of skill in the art would not recognize a core structure, common attributes, or features of the inhibitors. One of skill in the art would not recognize the inhibitors outside of those specifically identified. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to be an inhibitor. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and

thus that the applicant was not in possession of the claimed genus. As discussed above, the genus of possible peptides includes over 10995116277760000000000000000000000000000000000000 peptides (i.e. peptides of formula Met-(Xaa)20-Ala-(Xaa)20-Pro where each Xaa can be any of the 20 naturally occurring amino acids (compare claim 1d)). It is unclear which of these peptides exhibit the claimed activity. Further, the claims recite SEQ ID NO:1 Met-Ala-Pro and SEQ ID NO:2 Ile-His-Ala. However, Met-Ala-Pro and Ile-His-Ala do not share a structural core.

(5) Method of making the claimed invention/actual reduction to practice:

The specification (examples 1-3) describes the making of inhibitor peptides. However, such compounds are not representative of the breadth of the instant genus nor do the compounds provide a specific correlation between structure and function such that one could identify any and all inhibitors.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 11-16 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification

does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Reid et al (Appl Microbiol Biotechnol "comparison of bovine b-casein hydrolysis by P1 and Piii-type proteinases from Lactobacullus lactis subsp. cremoris" (1991) 36:344-351) teach that bovine beta-casein (abstract). In figure 4, Reid teach the peptide sequence of bovine beta-casein (page 348). Reid teach that amino acids 102-104 are Met-Ala-Pro (see also Table 11 peak 11). Thus the naturally occurring bovine beta-casein comprises Met-Ala-Pro (i.e. SEQ ID NO:1 of the instant invention) as recited in the instant claims. Further, since the peptide is present in

the bovine it is necessarily present in a composition as recited in the instant claims. It is noted that applicants own specification acknowledges that particular peptides are found in casein (page 2 lines 13-16).

There is no indication that the peptides/inhibitors of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Reid et al (Appl Microbiol Biotechnol "comparison of bovine b-casein hydrolysis by P1 and Piii-type proteinases from Lactobacullus lactis subsp. cremoris" (1991) 36:344-351) .

Reid et al (Appl Microbiol Biotechnol (1991) 36:344-351) teach that bovine beta-casein hydrolysis was compared by using various proteinases (abstract). In figure 4, Reid teach the peptide sequence of bovine beta-casein (page 348). Reid teach that amino acids 102-104 are Met-Ala-Pro (page 348). Thus the naturally occurring bovine beta-casein comprises Met-Ala-Pro (i.e. SEQ ID NO:1 of the instant invention) as recited in the instant claims. Further, Reid teach that specific digested portions of the beta-casein were isolated (see Table 1) and in figure

7a (page 349) state that residues 193-209 of the casein are in peak 11. Reid teach that HPLC peak 11 contains the peptide comprising Met-Ala-Pro (Table 1). As such, the peptide was necessarily in a composition as recited in claims 14,16. It is noted that claim 12 recites that the peptide is an inhibitor for an angiotensin-converting enzyme. Since Reid teach the peptide such peptide would have the claimed property (see MPEP section 2112.01). It is noted that claim 13 recites the words 'food or drink'. Since Reid teach that HPLC peak 11 contains the peptide comprising Met-Ala-Pro (Table 1) such composition is in a form suitable for food or drink. It is noted that claims 15-16 recite that the agent is for preventing and/or treating diseases. Such statement regarding the use is an intended use as it does not limit the composition to a particular structure. Thus Reid teach the limitations of claims 11-16 of the instant invention.

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen (US 2002/0172692).

Cohen teach (page 5, SEQ ID NO:3) the peptide Met-Ala-Pro as recited in the instant claims. It is noted that claim 12 recites that the peptide is an inhibitor for an angiotensin-converting enzyme. Since Cohen teach the peptide such peptide would have the claimed property (see MPEP section 2112.01). Cohen further teach that the peptide Met-Ala-Pro is part of a protein designated RTS (section 0010,0012) which is used as an antigen (section 0020-0021). As such, the peptide was necessarily in a composition as recited in claims 14,16. It is noted that claim 13 recites the words 'food or drink'. Since Cohen teach the peptide as part of a composition (section 0021 for example) it is in a form suitable for food or drink. It is noted that

claims 15-16 recite that the agent is for preventing and/or treating diseases. Such statement regarding the use is an intended use as it does not limit the composition to a particular structure. Thus Cohen teach the limitations of claims 11-16 of the instant invention.

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Parry et al (WO 02/098448).

Parry teach amino acid sequences that modulate ACE-2 (angiotensin converting enzyme 2) (abstract). Parry teach the peptide RGHCRDSRCMMNAPG (SEQ ID NO:89 page 9, SEQ ID NO:69 page 174) which comprises MAP (RGHCRDSRCMMNAPG) in which one or more amino acids are added (RGHCRDSRCM at the N-terminus, N in between M and AP, and G at the C-terminus). Thus Parry teach peptides as recited in instant claim 11d. It is noted that claim 11d-12 state that the peptide inhibits angiotensin-converting enzyme. Parry teach peptides which meet the structural limitations, thus absence evidence to the contrary Parry meet the claimed limitations. Further, Parry teach that the amino acid sequences modulate ACE-2 (angiotensin converting enzyme 2) (abstract). Since Parry teach the peptides as part of phage binding experiments (page 173) the peptides were present in compositions as recited in the instant claims 14,16. It is noted that claim 13 recites the words 'food or drink'. Since Parry teach the peptide as part of a composition (section 0021 for example) it is in a form suitable for food or drink. It is noted that claims 15-16 recite that the agent is for preventing and/or treating diseases. Such statement regarding the use is an intended use as it does not limit the composition to a particular structure. Thus Parry teach the limitations of claims 11-16 of the instant invention.

Prior art of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Chang et al WO 01/27242 as cited in IDS dated 2/23/07. As noted in the restriction requirement (dated 3/30/09) Chang teach peptides in claim 11 including peptides of sequence Met-Ala-Pro.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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